Complications of Pelvic Lymphadenectomy: Do the Risks Outweigh the Benefits?

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The American Urological Association Best Practice Policy states that although pelvic lymph node dissection (PLND) is commonly done with radical prostatectomy, its morbidity must be considered, particularly in cases in which it offers little additional information. The benefits of PLND include more accurate staging and reassurance for the patient. In addition, PLND may be therapeutic for men with lymph node metastases and may result in long-term biochemical cure for selected node-positive patients. However, the incidence of node positivity is declining, and accordingly a greater number of lymphadenectomies must be performed to benefit 1 patient. In addition to the associated cost, PLND has the potential for morbidity, including lymphoceles, thromboembolic events, ureteral injury, and neurovascular injury. Patients and physicians should therefore assess the risk/benefit ratio associated with PLND on an individual basis to permit informed treatment decisions. [Rev Urol. 2010;12(1):20-24 doi:10.3909/riu0422]

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> elvic lymph node dissection (PLND) is the gold standard for the detection of occult nodal metastases from prostate cancer. The traditional dissection includes the removal of nodal tissue between the external iliac vein and obturator nerve, extending laterally to the pelvic sidewall. However, a more extended approach is performed at many institutions. Both the lymph node yield¹ and the risk of complications² are highly dependent on the extent of PLND. The most

common complications after PLND are lymphocele formation, thromboembolic events, vascular injury, nerve injury, and ureteral injury. In addition to the potential for morbidity, PLND adds an estimated \$900 to \$3000 to the cost of radical prostatectomy, both for the additional operative time and pathologic consultation fees.^{3,4}

As the frequency of nodal metastases has precipitously declined during the prostate-specific antigen (PSA) era, it is possible that the risk to benefit ratio of PLND may have changed. This article reviews the complications associated with PLND in an effort to better delineate the potential advantages and disadvantages associated with this procedure in the contemporary era.

Potential Benefits of Pelvic Lymphadenectomy

Important advantages of PLND are accurate staging and patient peace of mind. In the 1970s and 1980s, as many as 20% to 40% of patients with apparently localized prostate cancer had positive lymph nodes.⁵ However, this fraction has decreased to less than 4% today, corresponding to the widespread use of PSA-based screening. Using the D'Amico risk groups,6 Kawakami and colleagues⁷ reported lymph node metastases in 0.87% of low-risk, 2.0% of intermediate-risk, and 7.1% of high-risk patients.

Correspondingly, fewer pelvic lymph node dissections are being performed in the community than in the past. According to observational data from the Cancer of the Prostate Strategic Urologic Research Endeavor, 94% of radical prostatectomy patients underwent PLND from 1992 to 1994, compared with only 80% by 2001.7 The most substantial decreases occurred in the low- and intermediaterisk groups, whereas the rate of PLND among high-risk patients remained relatively stable over time.

There may also be a therapeutic benefit associated with PLND, although this subject remains controversial. Indeed, a proportion of patients with lymph node metastases may be cured with complete surgical excision alone. At a median of 7.1 years after radical prostatectomy and PLND, Messing and coworkers8 re-

cant. Stratified by D'Amico risk classifications, the failure-free rates were also similar between the groups. Weight and colleagues 10 likewise reported no difference in biochemical progression-free survival between men who underwent limited PLND versus no PLND (P = .3). Nevertheless, because neither study was

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ported that 17% of men with nodepositive prostate cancer were alive with undetectable PSA in the absence of secondary therapy.

Several recent observational studies have also attempted to determine whether PLND has a therapeutic advantage. Allaf and colleagues1 compared the cancer control outcomes between 1865 men who underwent limited PLND and 2135 men who had a more extended PLND. Not surprisingly, patients in the extended PLND group had significantly more nodes removed, and a significantly greater proportion had lymph node metastases. There was a nonsignificant trend toward improved biochemical survival rates among men who had a more extensive lymph node dissection. Because of the small number of men with lymph node metastases in both groups, it is possible that there was not enough power to detect a statistical difference.

Using a different study design, Berglund and associates9 compared the outcomes of men who underwent a limited PLND with those of similar patients who did not have PLND at all. The primary outcome measure in this study was biochemical failure or the initiation of secondary therapy. At 5 years the failure-free rates were 74% and 70% in the PLND and no-PLND groups, respectively, a difference that was not statistically signifiprospectively randomized, it is possible that PLND was performed more frequently in patients with higher risk features. In this case, an alternate explanation is that the absence of a survival difference may instead represent a benefit from the node dissection.

If there is indeed a survival advantage associated with removal of positive regional lymph nodes, presumably the affected nodes must be contained within the PLND template. As discussed, a more extended PLND is associated with a higher likelihood of encountering positive lymph nodes but also a greater risk of complications. Unfortunately, lymphatic drainage from the prostate has considerable variability. Indeed, Mattei and associates¹¹ recently showed that only 38% of the primary lymph nodes were located within the obturator fossa, and even an extended PLND template may miss up to 33% of potential primary landing sites.

Finally, a substantial number of "unnecessary" lymphadenectomies must be performed to potentially improve the outcomes for a small fraction of patients. Klein and colleagues12 estimated the number needed to treat (NNT) for PLND to prevent 1 clinical event. Assuming that removal of 100% of the primary lymph nodes causes a 15% decrease in the rate of clinical events, the NNT was 667 for patients with a 1% likelihood of positive lymph nodes. By contrast, for men with a 10% likelihood of positive lymph nodes, the NNT was 67 to potentially "cure" 1 patient. Clearly, the preoperative probability of lymph node metastases should be an important consideration for clinical decision making regarding PLND.

Complications of Pelvic Lymphadenectomy

Although PLND is generally considered a relatively benign procedure, several complications may occur and may vary considerably in their severity. In this section, we review the most frequent complications in detail, including the frequency, presentation, and management.

Lymphocele

Lymphoceles are lymph-filled collections without a distinct epithelial lining, caused by the disruption of efferent lymphatics during PLND.13 Although they are among the most common complications from PLND, their presentation is highly variable. Patients may be asymptomatic, or present with pain, fever, genital or lower extremity edema, or urinary and gastrointestinal symptoms from mass effect on adjacent organs.

Several factors have been identified that may increase the risk of lymphocele after PLND. Surgical technique can contribute to lymphocele risk, such as the excessive use of diathermy.14 Other important surgical factors are the extent of PLND (extended > limited) and, in particular, the disruption of the lymphatics overlying the external iliac artery. Other factors that have been associated with an increased lymphocele risk include prior radiation therapy and subcutaneous heparin.13

The initial description of lymphocele after urologic surgery was by

Table 1 Lymphocele Rates in Contemporary Radical Prostatectomy Series With Limited Versus Extended Pelvic Lymph Node Dissection

Study	Limited	Extended
Allaf et al. ¹	-	3 (0.1)
Briganti et al. ²⁶	9 (4.6)	79 (10.3)
Clark et al. ²¹	1 (0.8)	3 (2.4)
Heidenreich et al. 19	9 (9)	9 (10.6)
Musch et al. ²	29 (3.3)	41 (9.4)

Values are number represented as whole numbers with the percentage in parenthesis.

Basinger and Gittes in 1975. In 1981. Sogani and colleagues13 reported a 4.7% lymphocele rate among 187 patients who underwent PLND for either prostate or bladder cancer. Table 1 shows published rates of lymphocele formation in contemporary radical prostatectomy series, stratified by the extent of PLND. Although the borders of PLND varied somewhat between studies, it is clear that in each population a more extensive dissection was associated with a greater risk of lymphocele formation. It is also noteworthy that some groups performed routine sonography on all patients before discharge, which may have increased the diagnosis of clinically "insignificant" lymphoceles. Indeed, studies from the radiologic literature have reported much higher rates of subclinical lymphoceles when routine imaging was performed after PLND, irrespective of symptoms. For example, Spring and colleagues¹⁶ reported a 22% rate of lymphoceles on routine ultrasound after open PLND for prostate cancer. Solberg and associates¹⁷ instead performed routine computed tomography scans on 132 patients after PLND for prostate cancer. The overall rate of lymphoceles was 54%. Fortunately very few of these cases were 5 cm or larger, and even fewer caused any clinical consequence.

There are many different management options for lymphoceles. Small asymptomatic collections can be managed conservatively. Studies using this approach have demonstrated absorption over time with bed rest and antibiotics alone. 16 Another option is simple aspiration, although fluid reaccumulation may occur, and there is an associated risk of infection.13 Sclerotherapy has also been described using various chemical agents, such as povidone-iodine, diatrizoate meglumine, and doxycycline. Surgical options include marsupialization into the peritoneal cavity, which may be performed using an open or laparoscopic percutaneous approach. Finally, drainage has become an increasingly popular form of management and is particularly useful in the setting of suspected infection.

Thromboembolic Events

Deep venous thrombosis and/or pulmonary embolism have been reported in approximately 0% to 8% of modern PLND series. 18,19 Particularly concerning is the association between lymphocele and an increased risk of thromboembolic events. For example, in the recent series by Musch and colleagues,2 deep venous thrombosis and pulmonary embolism occurred in 8.3% and 2.8% of patients with lymphoceles, respectively, compared with less than 1% of the patients without a lymphocele (P = .001).

Further complicating this situation is the association between prophylactic heparin and a higher risk of lymphocele formation. Catalona and coworkers²⁰ reported lymphoceles in 38% of patients given mini-dose heparin, compared with only 3% of patients who did not receive heparin. The investigators suggested that heparin may increase the risk of lymphocele through a delay in the clotting of lymph.

Our institution does not use prophylactic heparin for average-risk patients undergoing radical prostatectomy with PLND. However, sequential compression devices and early ambulation should be encouraged to reduce the frequency of thromboembolic complications.

Ureteral Injury

The ureter is a retroperitoneal structure that enters the pelvis in the region of the bifurcation of the common iliac artery. Once over these vessels, it courses along the inferiorlateral pelvis into the bladder. Injuries to the ureter are a relatively infrequent complication of PLND, occurring in less than 1% of large series. 2,19,21-23 The type of PLND (open or laparoscopic) does not seem to impact the incidence of this rare injury. Extended lymph node dissection was associated with high complication rates

in a report by Stone and colleagues²³; however, this association was not observed in other large series. 1,19

Most ureteral injuries are recognized at the time of PLND.² Repair generally involves mobilization of the proximal end of the cut ureter with reimplantation into the bladder over a ureteral stent. Reimplantation into the base of the bladder is gener-

The obturator nerve can sustain either a transection or crush injury during PLND. This is reported in 0 to 5.1% of recent series, with a higher frequency observed in several early series of laparoscopic PLND. 22,23 More recent, larger laparoscopic series have reported lower rates, similar to those in open series (0%-1.8%).^{24,25} If recognized intraoperatively, the nerve

The obturator nerve can sustain either a transection or crush injury during PLND.

ally preferred, because this region of the bladder is more fixed than the dome, and there is less chance of ureteral kinking during bladder filling. The optimal type of reimplantation (refluxing or nonrefluxing) has not been well studied in this clinical setting. Precise dissection, identification of anatomic landmarks, and the avoidance of blind soft tissue clipping can reduce the risk of ureteral injury.

Neurologic Injury

The most common neurologic tissue injured in PLND is the obturator nerve. It provides sensory innervation to the skin on the medial aspect of the thigh, as well as motor innervation of the adductor muscles in the thigh. The obturator nerve enters the pelvis behind the iliac arteries, runs laterally along the pelvic sidewall, and exits via the obturator foramen.

injury should be managed by either removing the suspect clip or reapproximating the severed nerve with fine (5-0 or 6-0) nonabsorbable suture. Postoperative management consists of intensive physical therapy.

Vascular Injury

The lymphatics that drain the prostate are surrounded by major vascular structures, including the external and internal iliac artery and vein. Nevertheless, vascular complications are relatively uncommon, and substantial blood loss due solely to injury of a major pelvic vessel during PLND has not been reported in most recent series.

The obturator vessels, which often run in parallel with the obturator nerve, may also be injured during the PLND. If such an injury is noted intraoperatively, ligation should be performed to prevent a delayed bleed.

Main Points

- Pelvic lymph node dissection (PLND) is the gold standard for the detection of occult nodal metastases from prostate cancer. The traditional dissection includes the removal of nodal tissue between the external iliac vein and obturator nerve, extending laterally to the pelvic sidewall.
- Important advantages of PLND are accurate staging and patient peace of mind. There may also be a therapeutic benefit associated with PLND, although this subject remains controversial.
- The most common complications after PLND are lymphocele formation, thromboembolic events, vascular injury, nerve injury, and ureteral injury.

Conclusions

The American Urological Association Best Practice Policy states that although PLND is commonly done with radical prostatectomy, its morbidity must be considered, particularly in cases in which it offers little additional information. Furthermore, patients with a PSA value < 10 ng/mL and Gleason score of \leq 6 rarely have lymph node metastases, so it is appropriate to omit lymphadenectomy in this group.

The benefits of PLND include more accurate staging and reassurance for the patient. In addition, PLND may be therapeutic for men with lymph node metastases and may result in longterm biochemical cure for selected node-positive patients.

However, the incidence of node positivity is declining, and accordingly a greater number of lymphadenectomies must be performed to benefit 1 patient. In addition to the associated cost, PLND has the potential for morbidity, including lymphothromboembolic ureteral injury, and neurovascular injury. Patients and physicians should therefore assess the risk to benefit ratio associated with PLND on an individual basis to permit informed treatment decisions.

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